



## Clinical trial results:

### A Safety study of Nivolumab in Patients with Recurrent and/or Metastatic Platinum-refractory Squamous Cell Carcinoma of the Head and Neck (SCCHN).

#### Summary

EudraCT number	2017-000424-10
Trial protocol	FR
Global end of trial date	27 May 2022

#### Results information

Result version number	v1 (current)
This version publication date	28 June 2025
First version publication date	28 June 2025

#### Trial information

##### Trial identification

Sponsor protocol code	UC-0130/1703
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03226756
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75015
Public contact	Nourredine AIT RAHMOUNE,, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.fr
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Notes:

##### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 February 2021
Global end of trial reached?	Yes
Global end of trial date	27 May 2022
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To estimate the incidence of high-grade (i.e. Grade 3-5 of CTCAE v4.0) adverse events of interest (AEI) in patients with recurrent and/or metastatic platinum refractory SCCHN treated with nivolumab in monotherapy. AEI are defined as adverse reactions known to be related to nivolumab (i.e. skin, endocrinopathy, gastrointestinal, hepatic, renal, pulmonary, and hypersensitivity adverse events) and other adverse events not related to carcinoma progression or to intercurrent disease clearly identified.

Protection of trial subjects:

This study was conducted in accordance with the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice (GCP) Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) and the applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 July 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	France: 343
Worldwide total number of subjects	343
EEA total number of subjects	343

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	198

From 65 to 84 years	140
85 years and over	5

## Subject disposition

### Recruitment

Recruitment details:

351 patients were included from 07-AUG-2017 to 05-NOV-2018 by 28 recruiting centers . Among them, eight patients were not treated: two did not receive any cure because of the appearance of brain metastasis before the first treatment, four of them died and the last one presented an adverse event clinically significant before their first treatment.

### Pre-assignment

Screening details:

In this study, patients presented recurrent and/or metastatic platinum-refractory Squamous Cell Carcinoma of the Head and Neck (SCCHN) were included. Following the signature of the informed consent form, all included patients received nivolumab treatment until immune Confirmed Progressive Disease (iCPD) the patients were followed-up for two years.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Nivolumab 3 mg/kg, every 2 weeks
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Arm description:

All patients enrolled in the study will received Nivolumab injections, 3mg/kg IV, every 2 weeks, up to 12 cycles (1 cycle = 28 days) until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab isotonic aqueous solution (10 mg/mL) intravenously injected over  $30 \pm 5$  min. to a final dose of 3 mg/kg, every two weeks for n cycles until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.

<b>Number of subjects in period 1</b>	Nivolumab 3 mg/kg, every 2 weeks
Started	343
Completed	6
Not completed	337
Consent withdrawn by subject	6
Physician decision	11
Death	54
Other	17
Adverse event	25

Progressive disease	223
Protocol deviation	1

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial (overall period)
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Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	343	343	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	198	198	
From 65-84 years	140	140	
85 years and over	5	5	
Age continuous Units: years			
median	62		
inter-quartile range (Q1-Q3)	56 to 69	-	
Gender categorical Units: Subjects			
Female	64	64	
Male	279	279	
ECOG Units: Subjects			
ECOG 0	84	84	
ECOG 1	206	206	
ECOG 2	52	52	
Missing	1	1	
Primary site of cancer Units: Subjects			
Hypopharynx	68	68	
Larynx	52	52	
Oral cavity	83	83	
Oropharynx	138	138	
Unknown primary	2	2	
Metastatic disease Units: Subjects			
No	126	126	
Yes	217	217	
Loco regional Recurrent disease Units: Subjects			
No	102	102	

Yes	241	241	
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## End points

### End points reporting groups

Reporting group title	Nivolumab 3 mg/kg, every 2 weeks
Reporting group description: All patients enrolled in the study will received Nivolumab injections, 3mg/kg IV, every 2 weeks, up to 12 cycles (1 cycle = 28 days) until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.	

### Primary: Time until Grade 5 SADR occurre

End point title	Time until Grade 5 SADR occurre <sup>[1]</sup>
End point description: The primary endpoint of this study was to assess the incidence of nivolumab induced Grade 3, 4 and 5 ADRs and SADRs susceptible to promote skin, endocrinologic, gastrointestinal, hepatic, renal, pulmonary, or hypersensitivities as well as other AEs not related to either carcinoma progression or clearly identified intercurrent disease.  The 5 Grade 5 SADRs were recorded and consisted of 3 interstitial lung disease, 1 autoimmune hepatitis, and 1 cardi-respiratory arrest.	
End point type	Primary
End point timeframe: Last day dose + 100 d	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analysis to report for this end point.	

End point values	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Months				
number (not applicable)				
Interstitial lung disease 1	0.7228			
Autoimmune hepatitis	1.7413			
Interstitial lung disease 2	10.3491			
Interstitial lung disease 3	1.2813			
Cardio-respiratory arrest	0.2628			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description: Overall survival is defined as the time from date of inclusion to date of death due to any cause. Patients last known to be alive will be censored at date of last contact. Overall survival will be estimated by	

Kaplan Meier method.

End point type	Secondary
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End point timeframe:

Up to 36 months.

<b>End point values</b>	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Months				
median (confidence interval 95%)	7.4 (6.5 to 8.9)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)
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End point description:

Progression-free survival is defined as the time since the inclusion in the trial to the first event among progression and death, whatever the cause of death. Progression is defined according to RECIST 1.1. Patients last known to be alive without progression having occurred before will be censored at date of last contact. Progression free survival will be estimated by Kaplan Meier method.

End point type	Secondary
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End point timeframe:

Up to 36 months.

<b>End point values</b>	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Months				
median (confidence interval 95%)	1.8 (1.8 to 1.9)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Objective response rate (ORR) (complete response and partial response according to RECIST 1.1 and to iRECIST) during nivolumab treatment

End point title	Objective response rate (ORR) (complete response and partial
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response according to RECIST 1.1 and to iRECIST) during nivolumab treatment

End point description:

The rate of patients with objective response (complete response or partial response) will be provided. The response is the best response obtained at the evaluations performed during treatment and at the end of treatment. Two evaluations of the response will be done: one according to the RECIST 1.1 criteria and one according to the Immune-related Response Criteria (iRECIST).

End point type Secondary

End point timeframe:

The time between the first dose of treatment until the best response, assessed up to 36 months.

<b>End point values</b>	Nivolumab 3 mg/kg, every 2 weeks			
Subject group type	Reporting group			
Number of subjects analysed	343			
Units: Patients				
Not evaluated N	67			
Progressive disease N	145			
Stable disease N	74			
Partial response N	45			
Complete response N	12			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The period of observation of adverse events of interest was the period of nivolumab treatment and 180 days after.

Adverse event reporting additional description:

For non serious adverse events the number of occurrence are not available and will be always noted "1"

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	Nivolumab 3 mg/kg, every 2 weeks
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Reporting group description:

All patients enrolled in the study will received Nivolumab injections, 3mg/kg IV, every 2 weeks, up to 12 cycles (1 cycle = 28 days) until of immune Confirmed Progressive Disease (iCPD) according to iRECIST guidelines.

<b>Serious adverse events</b>	Nivolumab 3 mg/kg, every 2 weeks		
Total subjects affected by serious adverse events			
subjects affected / exposed	181 / 343 (52.77%)		
number of deaths (all causes)	291		
number of deaths resulting from adverse events	10		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastric carcinoma			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lung metastases			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastatic bone pain			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal cancer			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumor bleeding			
subjects affected / exposed	15 / 343 (4.37%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 5		
Tumor hemorrhage			
subjects affected / exposed	13 / 343 (3.79%)		
occurrences causally related to treatment / all	1 / 14		
deaths causally related to treatment / all	0 / 7		
Tumor pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tumor progression			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tumour bleeding			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Acute limb ischaemia			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Aortic stenosis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Bleeding</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cerebral infarction</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hemoptysis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Hemorrhage</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Ischemic stroke</b>			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
<b>Jugular vein thrombosis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Pulmonary embolism</b>			

subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Tumor hemorrhage</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Surgical and medical procedures</b>			
<b>Scar revision</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>TAVI</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Surgery</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>General disorders and administration site conditions</b>			
<b>Asthenia</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Death</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Disease progression</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

Fever			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	20 / 343 (5.83%)		
occurrences causally related to treatment / all	1 / 20		
deaths causally related to treatment / all	1 / 9		
Hyperthermia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	6 / 343 (1.75%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 3		
Sudden death			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	3 / 3		
Unknown cause of death			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adult respiratory distress syndrome			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

Aspiration pneumonia				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchial congestion				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchial obstruction				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease exacerbation				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Dyspnea				
subjects affected / exposed	7 / 343 (2.04%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Food aspiration				
subjects affected / exposed	1 / 343 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemoptysis				
subjects affected / exposed	2 / 343 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Inhalation pneumonia				

subjects affected / exposed	4 / 343 (1.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Interstitial lung disease</b>			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	2 / 2		
<b>Interstitial pneumonia</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Interstitial pneumonitis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
<b>Laryngeal dyspnea</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Laryngeal oedema</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Lung infection</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Oropharyngeal hemorrhage</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Plaural effusion</b>			

subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 1		
<b>Pneumonitis</b>			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
<b>Pneumopathy</b>			
subjects affected / exposed	9 / 343 (2.62%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 3		
<b>Pneumothorax</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory distress</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory tract hemorrhage</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Psychiatric disorders</b>			
<b>Anxiety</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Suicide attempt</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Psychiatric decompensation</b>			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Product issues</b>			
<b>Catheter dislodgment</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Prosthetic cardiac valve leakage</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Investigations</b>			
<b>Troponin increased</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Weight loss</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Injury, poisoning and procedural complications</b>			
<b>Arm fracture</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Bleeding postoperative</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Drug overdose</b>			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Fall			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrostomy tube site complication			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hemopneumothorax			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leg fracture			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 1		
Subdural hematoma			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tracheal obstruction			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular access complication			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac arrest			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Coronary artery stenosis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Myocardial infarct</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Myocardial infarction</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Takotsubo syndrome</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Nervous system disorders</b>			
<b>Coma</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Consciousness loss</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Convulsion</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Epilepsy</b>			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Facial paralysis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Generalized tonic-clonic seizure</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Headache</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Motor deficit</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Polyradiculoneuritis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Transient ischemic attack</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Blood and lymphatic system disorders</b>			
<b>Eosinophilia</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Thrombopenia</b>			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Gastrointestinal disorders</b>			
<b>Bleeding mouth</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Bowel obstruction</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Colitis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Diarrhea</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Dysphagia</b>			
subjects affected / exposed	5 / 343 (1.46%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
<b>Femoral hernia strangulated</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hemorrhoids</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Inguinal hernia</b>			

subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mouth pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal fistula			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral hemorrhage			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain esophageal			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tongue bleeding			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vomiting			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hepatobiliary disorders</b>			
Acute cholecystitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Autoimmune hepatitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Hepatitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis autoimmune			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Skin and subcutaneous tissue disorders</b>			
Zona			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Renal and urinary disorders</b>			
Renal colic			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Acute renal insufficiency			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophysitis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Hypothyroidism			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
SIADH			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dorsal pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Osteoarthritis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in hip			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Bone infection			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchial infection			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary infection			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Catheter infection			
subjects affected / exposed	5 / 343 (1.46%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Catheter related infection			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis of face			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 1		
Device related infection			

subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Encephalitis</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Gastrointestinal infection</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infection</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infectious pneumonitis</b>			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Influenza</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Lung infection</b>			
subjects affected / exposed	7 / 343 (2.04%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 2		
<b>Pneumonia</b>			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	1 / 2		
<b>Pulmonary sepsis</b>			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Sepsis</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Staphylococcus aureus septicemia</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Staphylococcus epidermidis infection</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Superinfection</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Upper respiratory infection</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Metabolism and nutrition disorders</b>			
<b>Anorexia</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Decreased appetite</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
<b>Hypercalcemia</b>			

subjects affected / exposed	12 / 343 (3.50%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 3		
<b>Hypokalemia</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hyponatremia</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Malnutrition</b>			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
<b>Protein energy malnutrition</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Nivolumab 3 mg/kg, every 2 weeks		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	343 / 343 (100.00%)		
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>			
<b>Tumour haemorrhage</b>			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
<b>Tumour pain</b>			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
<b>General disorders and administration site conditions</b>			

Asthenia			
subjects affected / exposed	55 / 343 (16.03%)		
occurrences (all)	1		
Crepitations			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Feeling cold			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
General physical health deterioration			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hyperthermia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Mucosal inflammation			
subjects affected / exposed	14 / 343 (4.08%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	5 / 343 (1.46%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	10 / 343 (2.92%)		
occurrences (all)	1		
Xerosis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Immune system disorders			
Hypersensitivity			

subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Angular cheilitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Folliculitis subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Herpes Zoster subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Encephalitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Reproductive system and breast disorders			
Gynaecomastia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Pruritus genital subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Cough subjects affected / exposed occurrences (all)	7 / 343 (2.04%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	9 / 343 (2.62%) 1		
Dyspnoea exertional			

subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Epistaxis			
subjects affected / exposed occurrences (all)	3 / 343 (0.87%) 1		
Interstitial lung disease			
subjects affected / exposed occurrences (all)	6 / 343 (1.75%) 1		
Lung disorder			
subjects affected / exposed occurrences (all)	4 / 343 (1.17%) 1		
Lung infiltration			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Pleural effusion			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Pneumonitis			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Productive cough			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Rales			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Rhinorrhoea			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Insomnia			
subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		

Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	4 / 343 (1.17%) 1		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	4 / 343 (1.17%) 1		
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Lipase increased subjects affected / exposed occurrences (all)	8 / 343 (2.33%) 1		
Transaminases increased subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Weight decreased subjects affected / exposed occurrences (all)	3 / 343 (0.87%) 1		
Injury, poisoning and procedural complications			
Tracheostomy malfunction subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Congenital, familial and genetic disorders			

Phimosis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Deafness			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Ear pruritus			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Cyanosis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Stress cardiomyopathy			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Dysaesthesia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Dysarthria			

subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Dysgeusia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Headache subjects affected / exposed occurrences (all)	4 / 343 (1.17%) 1		
Hyperaesthesia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Loss of consciousness subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Neuropathy peripheral subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Paraesthesia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Polyneuropathy subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Somnolence subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Blood and lymphatic system disorders			
Anemia subjects affected / exposed occurrences (all)	17 / 343 (4.96%) 1		
Eosinophilia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		

Leukocytosis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Lymphopenia			
subjects affected / exposed	12 / 343 (3.50%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Eye disorders			
Lacrimation increased			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Aptyalism			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Colitis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	7 / 343 (2.04%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	18 / 343 (5.25%)		
occurrences (all)	1		
Dry mouth			

subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	19 / 343 (5.54%)		
occurrences (all)	1		
Oral pain			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	9 / 343 (2.62%)		
occurrences (all)	1		
Tongue oedema			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	6 / 343 (1.75%)		
occurrences (all)	1		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Cholestasis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Hepatocellular injury			
subjects affected / exposed	3 / 343 (0.87%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Dermatitis			

subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	11 / 343 (3.21%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Hyoerhidrosis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Night sweats			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Pemphigoid			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Pruritis			
subjects affected / exposed	19 / 343 (5.54%)		
occurrences (all)	1		
Pruritis generalised			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Psoriasis			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	11 / 343 (3.21%)		
occurrences (all)	1		
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Skin exfoliation			

subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Skin fissures subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Skin lesion subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Skin toxicity subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Xeroderma subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Renal failure subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Endocrine disorders			
Adrenal insufficiency subjects affected / exposed occurrences (all)	3 / 343 (0.87%) 1		
Hyperthyroidism subjects affected / exposed occurrences (all)	10 / 343 (2.92%) 1		
Hypophysitis subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Hypothyroidism subjects affected / exposed occurrences (all)	32 / 343 (9.33%) 1		
Inappropriate antidiuretic hormone secretion			

subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Thyroid disorder subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	7 / 343 (2.04%) 1		
Arthritis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Back pain subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Muscle spasms subjects affected / exposed occurrences (all)	2 / 343 (0.58%) 1		
Muscle tightness subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Musculoskeletal discomfort subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Musculoskeletal pain subjects affected / exposed occurrences (all)	3 / 343 (0.87%) 1		
Myalgia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Neck pain subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Pain in extremity			

subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Phabdomyolysis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
<b>Infections and infestations</b>			
Bronchitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Encephalitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Oral fungal infection subjects affected / exposed occurrences (all)	4 / 343 (1.17%) 1		
Rash pustular subjects affected / exposed occurrences (all)	3 / 343 (0.87%) 1		
Rhinitis subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
<b>Metabolism and nutrition disorders</b>			
Decreased appetite subjects affected / exposed occurrences (all)	10 / 343 (2.92%) 1		
Hypercalcaemia subjects affected / exposed occurrences (all)	3 / 343 (0.87%) 1		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 343 (0.29%) 1		
Hyperkalaemia			

subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypernatraemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypochloraemia			
subjects affected / exposed	1 / 343 (0.29%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	4 / 343 (1.17%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	2 / 343 (0.58%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2018	<ul style="list-style-type: none"><li>- Inclusion number increase to 250</li><li>- Nivolumab Investigator's Brochure update</li><li>- Investigators' list modification</li><li>- Addendum to the Information Note regarding the Informed Consent Form</li></ul>
10 April 2018	<ul style="list-style-type: none"><li>- Inclusion number increase to 350</li><li>- Supplemental ancillary biological study (galectine-9 measurement) for 100 subjects</li><li>- Investigators' list modification</li><li>- Update of both the Informed Consent Form and its Information Note</li></ul>
04 July 2018	<ul style="list-style-type: none"><li>- Protocol-related: Inclusion period extension from 12 to 18 months and Extended HPV status diagnosis to availability of archived or new tumor biopsies for oropharynx's SCC). Nivolumab therapeutic regimens and treatment duration/period: the maximum of 12 cycles was removed and replaced by "up to progression (immune Confirmed Progressive Disease (iCPD) using iRECIST)</li><li>- Investigators' list modification</li><li>- Update of both the Informed Consent Form and its Information Note</li><li>- Supplemental information regarding General Data Protection Regulations for included patients being either currently treated or followed</li></ul>
28 May 2019	<ul style="list-style-type: none"><li>- Investigator's Brochure update</li><li>- Investigators' list modification</li><li>- Supplemental information "C" intended to the included patients being either currently treated or followed</li></ul>
10 September 2019	<ul style="list-style-type: none"><li>- Investigator's Brochure update</li><li>- Addendum to both Informed Consent Form and its Information Note</li><li>- Investigators' list modification</li></ul>
13 September 2021	<ul style="list-style-type: none"><li>- Treatment modalities update leading to SmPC update</li><li>- Protocol and synopsis update: Follow-up period modification</li><li>- Addendum to both Informed Consent Form and its Information Note to include new follow-up period</li><li>- Investigator's Brochure update</li><li>- Investigators' list modification</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported